

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Martha G. Welch et al.	Confirmation No.:	8041
Application No.:	10/799,941	Art Unit:	1654
Filed:	March 11, 2004	Examiner:	Andrew D. Kosar
Title:	NOVEL MULTYPEPTIDE REGIMEN FOR THE TREATMENT OF AUTISTIC SPECTRUM, BEHAVIORAL, EMOTIONAL AND VISCERAL INFLAMMATION/AUTOIMMUNE DISORDERS		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.131

We, Martha G. Welch, David A. Ruggiero, and Muhammad Anwar, hereby declare as follows:

1. We are co-inventors of the subject matter claimed in the patent application having U. S. Serial No. 10/799,941.
2. We have been informed that the claims now pending in this application are directed to a pharmaceutical composition comprising a therapeutically effective amount of secretin in combination with a therapeutically effective amount of oxytocin.
3. We have been informed that pending claims of the '941 application have been rejected by the patent Examiner over Hollander (U.S. Pub. No. 2006/0105939) in view of an on-line NIH news alert ("The Use of Secretin to Treat Autism" Internet document), and further in view of Swain (E. Swain, Pharmaceutical and Medical Packaging News) and PIERCE (PIERCE Technical Resource Sheet TR0043.0 "Protein Stability and Storage").
4. We conceived of the pharmaceutical composition claimed in the '941 application at least prior to August 17, 2001 as evidenced by the experiments and notes included in the laboratory notebooks attached. A redacted copy of relevant lab notebook entries is attached as **Exhibit A**.
5. We diligently reduced the claimed invention to practice.
6. The claimed invention was conceived and reduced to practice in the United States.

7. The work described within this Declaration was performed by us, or on our behalf under our supervision.

8. We hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the patent in which this declaration is made.

Date: _____

Martha G. Welch

Date: 9-18-08

David A. Ruggiero
David A. Ruggiero

Date: _____

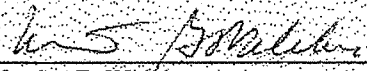
Muhammad Anwar

7. The work described within this Declaration was performed by us, or on our behalf under our supervision.

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Date:

9/16/08


Martha G. Welch

Date:

David A. Ruggiero

Date:

9-16-08



Muhammad Anwar

EXHIBIT A

SECRETIN

S-4

calcitonin

(Rat wt 275 g)

5 μ g in 10 μ l saline

injected slowly

Survival 24 hrs

Perfusion 4% PFA

X Secretin 1:5000

6 slides

S-5

calcitonin

(Rat wt 275 g)

5 μ g in 10 μ l saline

injected

as above

Oxy 1:5000

Secretin 1:5000

Double Secretin DAB Oxy Gold

Control 1:5000 Normal Rabbit Serum

S-6

Rat wt 455g (6 month old)

cannulated 4 days before injection

Secretin 5 μ g / 5 μ l PB a.m. x 3 interval 15 min

waited 3 hrs before perfusion

Perfused 4% PFA

Day 1

CFOS 1:8000

(to be retained for Micro

Double

CFOS / Oxy 1:5000

CFOS / Secretin 1:5000

CFOS / SHF 1:10000

used Biotin/ABC for CFOS

Used Peroxidase

conjugated IgG

4 μ l/ml for

oxy. Sec. & SHF

SECRETIN

S-7 (Rate 250/175g) cannulation 5 days before injections

AP = +7.0 mm

L = +1.8 mm

D = -3.0 mm (from G)

Double Dose

Secretin 10ug/sul x3 (15 mins interval)

CONTROL (NO Injection)

waited 3 hrs

Perfusion 4% PFA overnight fixative

Both animals entire brains to Frontal ex 3rd
T. spinal cord
Adrenal
Pituitary & Pineal

Processed for

CFOs - Nissl

CFOs - Oxy

eFos - Secretin

CFOs - CRH

Limited to PVN area

DATE: _____

TOPIC: SHR / WKY

TS - 13

Perfused

Processed

SHR

WKY

Medulla

cFos/Nissl

cFos/Nissl

cFos/PNMT

cFos/PNMT

cFos/R₁

cFos/R₁

Fore Brain

cFos/Nissl

cFos/Nissl

cFos/R₁

cFos/R₁

cFos/TH

cFos/TH

cFos/Secretin

cFos/Secretin

T₁

cFos/TH

cFos/TH

DATE: _____

TOPIC: _____

CP-52 (CONT)

(Perfused)

sagittal 16 μ

Animal Saline Pwp = 21.72g

Animal Cocaine 30.31g

Post fixed overnight with 3% PFA in 10% sucrose
cut on cryostat 5 μ thick

(Perfused)

4% PFA

overnight 10% sucrose

Saline 39.50g

cocaine 49.05g

cut coronal 30 μ

Order of collection & Processing

① Apoptosis

④ TH

② c-Fos

⑤ PMMT

③ GABA

⑥ Secretin

⑦ Oxytocin

Adrenal gland

c-Fos

c-Fos/TH

c-Fos/PMT

Head

Frozen for c-Fos/Apopt & TH

DATE:

TOPIC: Secretin/Oxy

CP-53

P-13 mother arrived on Tue
Plug

ONE DAY OLD (Exp) stressed by separation — 3 min
Reunited — 15 min
Separated — 3 min
Reunited — 15 min
Separated — 3 min
Reunited — 2 1/2 hrs

(CONT) NO separation

Sagittal Sections Thru Pineal & Pituitary glands
also Pancreas.

CFOS/TH Secretin oxy

4 DAYS OLD

in one pair Repeated the above procedure,

in second pair one baby separated for longer (14 days)
survived

12 DAYS OLD

Repeated the above procedure
Day One procedure.

14/20 days old

Both previously (11th day) stressed
and a new baby stressed
according to previous method and
presented for Sec, oxy, CFOS.

DATE:

TOPIC: Piglet (Secretin)

CP-59 / ~~Piglet~~ (only for Secretin) and ~~Secretin~~

6 days old ♂

Perfused 4% PFA (3 lit)

30 μ l Sections (FR Sagittal Medull Coronal)

PNMT 1:15000 (Medulla)

CART 1:10000 (Medulla, FR)

Sec 1:5000 (chemicon FR)

Sec 1:10000 (Pheix FR)

oxy 1:10000 (chemicon FR)

DATE: _____

TOPIC: Hypoxia

CP-60/PG-19

2 Piglet (10 days old)

performed on

Medulla Processed for

Fos / TH

Fos / PTH

Fos / TH

Fos / SHH

Tomy, Lisa

PG-19

Fore Brain

Double Label for

Fos / Secretin

Fos / oxytocin

DATE: _____

TOPIC: IBD

CP-63

6 Rat Ent approximately 225 remain on

4	for IBD	}
2	" CONT	

TWBS DOSE

Day 1 Enema Dose

Oxy 242 14/10/11

Day 3

Enema 242 14/10/11

Day 8

A12A Punks on

Animal	1.	CONT	no treatment
"	2.	CONT	Oxy + Sec
"	3.	IBD	Oxy + Sec
"	4.	IBD	Oxy
"	5.	IBD	Sec
"	6.	Did not	

Survived 5 days

Perforated 19/11 wad.

C 655 14/10/11

CONTIBD

PBS 200 ml
 Ethanol 500 ml

PBS - 200 ml
 TWBS - 300 ml
 100% Ethanol - 500 ml

1000 ml - 1 ml

1000 ml

DATE:

TOPIC: 136

CP-64

8 Rat 1BD ~~are~~ wt 250g

4 CONT
11 TNDS.

one cont did

TNDS

D0728

Doubled as of CP-63

oxy 0.84/100 ml

Sec 0.84

DATE:

TOPIC: Sec/Oxy Colelim

CP-65

Sec

2 Rats 2.5 μ l Colelim (15 mg / 1 ml Saline)
Survived overnight

Rats died